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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769,787	01/26/2001	Christophe Francois Guy Gilbert	031855.0091	4454

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HUNTON & WILLIAMS
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER
BASKAR, PADMAVATHI

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/16/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/769,787	GILBERT ET AL.	
	Examin r	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

1. The amendment filed on 3/20/03 Paper # 13 has been entered into the record. Claim 20 has been amended. New claims 21 and 22 have been added. Claims 1-22 are pending in the application.

2. The examiner acknowledges various amendments made to the Specification to obviate various informalities as set forth in the previous office action.

Priority

3. The examiner corrected the priority document as GB in the record and the priority will be accorded to GB 9816337.1 7/27/1998 after receiving the certified document.

Restriction

4. Applicant provisionally elected by phone on July 09, 2002; Paper # 11, Group V, claim 20 without traverse. However, Applicant now states that the elected claim 20 of group V is elected with traverse. The traversal is on the ground(s) that (a) the restriction requirement described on the phone differs from that of Paper # 11, (b) a method for inducing immune response (Group IV), a method for treatment and prophylaxis (Group V), and a method of determining whether a protein is anti-microbial target in vivo or in vitro (Group VI) do over lap in scope and should be examined together.

The examiner would consider the elected invention Group V, SEQ.ID.NO: 162 with traverse. However, the traversal on the grounds that inventions IV, V and VI are to be examined together is not found persuasive because Inventions IV, V and VI are different methods utilizing different method steps using different biological reagents, which result in different outcome as explained in the previous office action Paper # 11. Therefore, the restriction is considered proper and made it final.

It is noted that the restriction of one SEQ.ID.NO is not an election of species. The examiner made it clear on the record in paper # 11, paragraph 7 that the disclosed sequences are considered as patentably distinct and different inventions since each SEQ.ID.NO is distinct and given a specific sequence identification number i.e., SEQ.ID.NO containing different amino acids or nucleic acids.

These sequences are plurality of patentably distinct inventions with distinct nucleic acid or amino acid sequences as represented in Tables 2-4. Therefore election of a single disclosed sequence SEQ.ID.NO: 162 under 35 U.S.C. 121 is considered as a patentably distinct invention. MPEP 809.03, MPEP.808.01, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required. In the instant situation, the inventions of the Group V are drawn to distinct inventions as described in the previous Office Action. Restriction between the inventions is deemed to be proper for the reasons previously set forth.

Therefore, claims 20-21 are currently under examination with respect to SEQ.ID.NO: 162.

Rejections Withdrawn

5. In view of amendment to the claim 20, the rejection under 35 U.S.C. 101("use" is not one of the statutory classes of invention) is withdrawn.

6. In view of amendment to the claim 20, the rejection under 35 U.S.C. § 112, second paragraph is withdrawn for omitting the essential method steps.

Rejection Maintain d

7. The rejection of claim 20 as being vague for the recitation of "capable of " is maintained as set forth in the previous office action because as written it is difficult to determine the metes and bound of "capable of ". Does this agent treat or prevent the infection or not?

New Rejections Based on the Amendment

8. MPEP: 2173 states that claims must particularly point out and distinctly claim the Invention. The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention. In claim 20, tables 2-4 contain several sequences and there is no practical way of defining the invention clearly.

Claim Rejections - 35 USC § 112, first paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written

description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

The claims encompass a method for treatment or prophylaxis of S.pneumoniae infection comprising administering to a patient in need thereof an agent capable of antagonizing, inhibiting, or otherwise interfering with the function or expression of a protein or polypeptide as defined in Tables 2-4, wherein said agent induces an immune response in said patient to a polypeptide having a sequence comprising SEQ.ID.NO: 162. Claim 20 reads on use of any epitope of SEQ.ID.NO: 162 Review of the present specification, the art of record indicates that mice vaccinated with a protein SEQ.ID.NO: 162 survived longer than the controls (Figure 1). However, the mice are not protected from infection as claimed (i.e., a method for prophylaxis of S.pneumoniae infection). There is no written description support for administration of polypeptide SEQ.ID.NO: 162 that is capable of antagonizing, inhibiting, or otherwise interfering with the function or expression of any protein or polypeptide as defined in Tables 2-4. Further, agents capable of antagonizing, inhibiting, or otherwise interfering with the function or expression of a protein or polypeptide as defined in Tables 2-4 except SEQ.ID.NO: 162 have not been identified nor described. Presently, in order to practice the invention as claimed the artisan must first obtain the agents, polynucleotides and/or polypeptide sequences of the Tables 2-4 and use them in a method for treatment or prophylaxis of S.pneumoniae infection and the agent administered agent should antagonize inhibit, or otherwise interfere with the function or

expression of a protein or polypeptide from S.pneumoniae. The specification fails to teach that the agent, which is administered, is capable of antagonizing, inhibiting, or otherwise interfering with the function or expression of any protein or polypeptide. The claimed invention as a whole is not adequately described and is not conventional in the art as of Applicant's effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant case, the claimed embodiments of the polynucleotides/polypeptides sequences needed to use in the invention as claimed lack a written description. The specification fails to describe any polynucleotides or polypeptides encompassed in the claims with particularity to indicate that Applicants had possession of the claimed invention. The written description of a claim is evaluated on the basis of the claimed invention as a whole. Case law established that the requirement for written description relates to the subject matter defined by the claims. *In re Wright, 9 USPQ2d 1649 (Fed. Cir. 1989).* The skilled artisan cannot envision the detailed function of the claimed polynucleic acids or polypeptides necessary to practice the methods as claimed.

The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art **as of Applicants effective filing date**. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class.

10. Claims 20-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating S.pneumoniae infection comprising administering to a patient an agent, SEQ.ID.NO: 162, wherein said agent is an isolated polypeptide comprising the amino acid sequence SEQ.ID.NO: 162 that induces an immune response in said patient, does not reasonably provide enablement for a method for treatment or prophylaxis of S.pneumoniae infection comprising administering to a patient in need thereof an agent capable of antagonizing, inhibiting, or otherwise interfering with the function or expression of a protein or polypeptide as defined in Tables 2-4, wherein said agent induces an immune response in said patient to a polypeptide having a sequence comprising SEQ.ID.NO: 162 or fragments of SEQ.ID.NO: 162. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method for treatment or prophylaxis of S.pneumoniae infection comprising administering to a patient in need thereof an agent capable of antagonizing, inhibiting, or otherwise interfering with the function or expression of a protein or polypeptide as defined in Tables 2-4, wherein said agent induces an immune response in said patient to a polypeptide having a sequence comprising SEQ.ID.NO: 162

The instant claims are evaluated for scope of enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is a method for treatment or prophylaxis of S.pneumoniae infection comprising administering to a patient in need thereof an agent capable of antagonizing, inhibiting, or otherwise interfering with the function or expression of a protein or polypeptide as defined in Tables 2-4, wherein said agent induces an immune response in said patient to a polypeptide having a sequence comprising SEQ.ID.NO: 162. The method of prophylaxis thus requiring *in vivo* enablement for prevention of the infection. The specification discloses that mice administered with an isolated polypeptide comprising the amino acid sequence SEQ.ID.NO: 162 survived longer than the controls (Figure 1). However, the mice are not protected from infection as claimed (i.e., a method for prophylaxis of S.pneumoniae infection). Therefore, it is unclear whether this approach is feasible in the prevention of S.pneumoniae infection. Further, the specification provides no working examples demonstrating (i.e., guidance) enablement for any *in vivo* uses of any other agents capable of antagonizing, inhibiting, or otherwise interfering with the function or expression of a protein or polypeptide as defined in Tables 2-4. Further, these tables contain nucleic acid sequences that have not been shown to antagonize, inhibit, or otherwise interfere with the function or expression of a protein or polypeptide.

Claim 20 reads on use of any epitope (fragments) of SEQ.ID.NO: 162. The specification fails to teach an isolated polypeptide fragments of SEQ ID NO: 162 and it is noted that the claimed fragments do not exist as an invention independent of their function in encoding a protein, SEQ.ID.NO: 162. The specification is not enabled for any fragments of SEQ ID NO: 16 2 because 1) the specification fails to teach fragments that are able to function by binding to immune sera; 2) the specification fails to teach how to make and use fragments thereof that have an unknown and uncharacterized function; 3) the specification fails to teach what are the critical amino acid residues that can be modified and still achieve a fragment with functional

activity 4) the art teaches that proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition, one skilled in the art would have reason to doubt the validity and functionality of the function of such antigenic fragments of SEQ ID NO: 162, and 5) applicants have not displayed a nexus between the structure and function of the claimed fragments. As to points 1)- 5), the specification fails to provide a written description of any fragments of a bacterial protein sequence of SEQ ID N0: 162. The specification fails to teach the critical protein residues involved in the function of the protein SEQ ID NO: 162, such that the skilled artisan is provided no guidance to test, screen or make fragments of the protein comprising SEQ ID NO: 162.

The state of the prior art indicates that protein chemistry is probably one of the most unpredictable areas of biotechnology and is highly complex. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a priori and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid

substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of a single amino acid residue may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol, 1991, 5(7): 1755-67) teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis in proteins and such proteins differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition.

Thus, peptide (i.e., fragment of SEQ.ID.NO: 162) treatment of S.pneumoniae must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Claim Objections

11. MPEP 2173.05(s) Reference to Figures or Tables states that

Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted).

Reference characters corresponding to elements recited in the detailed description and the drawings may be used in conjunction with the recitation of the same element or group of elements in the claims. See MPEP § 608.01(m).

In claim 20, tables 2-4 contain several sequences and there is no practical way of defining the invention clearly.

Status of Claims

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on M-F (6:30A.M-4: 00 P.M.) First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar
7/10/03

James C Housel
JAMES HOUSEL 7/14/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600